

**ABSTRACT**

[0309] The present invention relates to compositions and methods which enhance the local and systemic uptake and delivery of oligonucleotides and nucleic acids via non-parenteral routes of administration. Pharmaceutical compositions comprising oligonucleotides disclosed herein include, for systemic delivery, emulsion and microemulsion formulations for a variety of applications and oral dosage formulations. It has also surprisingly been discovered that oligonucleotides may be locally delivered to colonic sites by rectal enemas and suppositories in simple solutions, *e.g.*, neat or in saline. Such pharmaceutical compositions of oligonucleotides may further include one or more penetration enhancers for the transport of oligonucleotides and other nucleic acids across mucosal membranes. The compositions and methods of the invention are utilized to effect the oral, buccal, rectal or vaginal administration of an antisense oligonucleotide to an animal in order to modulate the expression of a gene in the animal for investigative, therapeutic, palliative or prophylactic purposes.